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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,902	01/14/2002	Ping Gao	6239.N CP	5445

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EXAMINER	
SNEDDEN, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

KD

Office Action Summary	Application No.	Applicant(s)	
	10/047,902	GAO ET AL.	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) *50-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48, 60-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of invention I, claims 1-48 and 60-64 is acknowledged. Claims 49-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse. Claims 1-48 and 60-64 are under examination.

Specification

2. The use of the trademark Povidine has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology, polyvinylpyrrolidone (PVP).

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Information Disclosure Statement

The information disclosure statement contains Foreign document references that are not in English and where an English equivalent is not provided. These references will be considered upon the submission of an English translation or equivalent.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-43, and 60-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-43, and 60-63 is indefinite as it is unclear whether the substituted cellulosic polymer is a component of the emulsion or a component of the capsule wall as recited in claims 22-24. Is the substituted cellulosic polymer required in the self-emulsifying component? Or, is the substituted cellulosic polymer removed from the emulsion when it is part of the capsule as recited in claims 22-24? As indicated below, the prior art accounts for both embodiments.

Claim 63 recites the limitation "present in the fill liquid composition". There is insufficient antecedent basis for this limitation in the claim. It is not clear what the "fill liquid composition" is referring to.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipate by Straub *et al.* (US 6,610,317). Straub *et al.* teach a composition of paclitaxel, a surfactant, a solvent and a substituted cellulosic polymer. The surfactant of Straub *et al.* is taught as a surfactant or a wetting agent, and includes polyoxyethylene castor oil derivatives, for example (see column 3, line 7; column 4, lines 45 to column 5, line 40). The solvent of Straub *et al.* is taught as a solvent or a pore forming agent, and includes ethanol substantially removed to about 1%, for example (see column 2, column 6, lines 15 and 50). The substituted cellulosic polymer of Straub *et al.* is taught as cellulose dextran, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxy-propylmethyl cellulose,

carboxyethyl cellulose, or carboxymethyl cellulose (column 4, lines 19-21). Thus, the reference anticipates the claimed invention.

5. Claims 1-11, 21 and 64 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lambert *et al.* (US Patent 6,660,286).

Lambert *et al.* teach a paclitaxel composition comprising a formulations for self-emulsifying systems of 0.1-20% paclitaxel, 10-90% Vitamin E (surfactant), 10-90% PEG 400 or N-methyl-2-pyrrolidone (solvent), 5-50% TPGS, 5-50% a secondary hydrophilific surfactant, such as Polysorbates (Tween 80), Pluronics (Pluronic F127), Cremophor RH40 (PEG-40 hydrogenated castor oil) or Solutol HS-15 (see column 14, lines 21-32; regarding claims 1, 2, 4-6). For oral delivery, the paclitaxel composition is taught as being encapsulated in a water-soluble gelatin capsule, a cellulosic polymer (regarding claim 3 and 21).

Lambert *et al.* teach self-emulsifying systems of 0.1-20% paclitaxel and 10-90% of Vitamin E and other surfactants. A specific embodiment for the composition of Lambert *et al.* would comprise 10% paclitaxel and 30-80% surfactant, allowing for a ratio of 1:3 to 1:8, for example. Ratios of 1:20 are also envisioned. (Regarding claims 7-8.)

Lambert *et al.* teach the use of polyethylene glycol, PEG 400, as the solvent (regarding claims 9-11).

Thus, Lambert *et al.* expressly teach a composition of paclitaxel comprising a pharmaceutically acceptable surfactant (Vitamin E, TPGS, PEG-40 hydrogenated castor oil, Solutol HS-15) and a pharmaceutically acceptable solvent (PEG 400). What is missing from the

teachings of Lambert *et al.* is the express teaching of an additional component of a substituted cellulosic polymer in combination with the above ingredients.

In the alternative, it would have been obvious to have used both a solvent, such as PEG 400, and a substituted cellulosic polymer, such as Povidone, in the same composition because Lambert *et al.* teach that both solvents modify the solubility behavior of paclitaxel, and are thus both potential solvents (column 4, line 4). At column 3, line 67, Lambert *et al.* introduces povidone as a co-solubilizer. Thus, Lambert *et al.* teach PEG 400 and Povidine as useful for the same purpose.

Additionally, Lambert *et al.* suggests the use of Povidone as a co-solubilizer for another solvent, such as PEG 400, and therefore, it would have been obvious to add Povidone to the composistion of paclitaxel, a pharmaceutically acceptable surfactant (Vitamin E, TPGS, PEG-40 hydrogenated castor oil, Solutol HS-15) and a pharmaceutically acceptable solvent (PEG 400). Thus, it would have been anticipated if not obvious to add Povidone to solubilize paclitaxel and reduce concentrations of each solvent in order to reduce the potential negative effects seen with high concentrations of any one solvent (see Lambert *et al.*, columns 1-2). Thus, the claimed invention was anticipated if not obvious at the time it was made.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-14, 18, 21-24, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al.* (US Patent 6,660,286) in view of Kunz *et al.* (US 2002/0025979).

Lambert teach a paclitaxel composition comprising a formulations for self-emulsifying systems of 0.1-20% paclitaxel, 10-90% Vitamin E (surfactant), 10-90% PEG 400 or N-methyl-2-pyrrolidone (solvent), 5-50% TPGS, 5-50% a secondary hydrophilific surfactant, such as Polysorbates (Tween 80), Pluronics (Pluronic F127), Cremophor RH40 (PEG-40 hydrogenated castor oil) or Solutol HS-15 (see column 14, lines 21-32; regarding claims 1, 2, 4-6). Lambert *et al.* teach self-emulsifying systems of 0.1-20% paclitaxel and 10-90% of Vitamin E and other surfactants. A specific embodiment the composition of Lambert *et al.* would comprise 10% paclitaxel and 30-80% surfactant, allowing for a ratio of 1:3 to 1:8, for example. Ratios of 1:20 are also envisioned. (Regarding claims 7-8.) Lambert *et al.* teach the use of polyethylene glycol, PEG 400, as the solvent (regarding claims 9-11). For oral delivery, the paclitaxel composition is taught as being encapsulated in a water-soluble gelatin capsule, a cellulosic polymer (regarding claim 3 and 21). Thus, Lambert *et al.* expressly teach a composition of paclitaxel comprising a pharmaceutically acceptable surfactant (Vitamin E, TPGS, PEG-40 hydrogenated castor oil, Solutol HS-15) and a pharmaceutically acceptable solvent (PEG 400), contained in a gelatin capsule.

Lambert *et al.* does not teach the use of a substituted cellulosic polymer, such as HPMC, in the capsule wall, or as a binder or inactive filler within the capsule.

Kunz *et al.* teach an oral composition of Taxol, or paclitaxel. Kunz *et al.* teach the standard formulation present in the art as containing inactive ingredients such as cellulose,

hydroxypropyl methylcellulose (HPMC) and microcrystalline cellulose (see Section [0168]; regarding claims 12-14, 18, 21-24). Hard or soft gelatin capsules containing paclitaxel can contain inactive ingredients, for example, gelatin and microcrystalline cellulose, as well as liquid vehicles such as polyethylene glycols (PEGs) and vegetable oil (see Section [0168]).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use HPMC as a component of the capsule. The person of ordinary skill in the art with been motivated to use HPMC, and would have expected success, as HPMC is a routine and standard part of the oral capsule formulations. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

8. Claims 1, 2 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al.* (US Patent 6,660,286) in view of Kunz *et al.* (US 2002/0025979) as applied to claims 1 and 2 above, and further in view of Broder *et al.* (US 6,395,770). Broder *et al.* oral doses of paclitaxel from 20 to 1000 mg/m^2 or about 2-30 mg/kg (see column 12, lines 25-50). Broder *et al.* teach that this is the range for a therapeutically effective dose for paclitaxel responsive diseases.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to formulate paclitaxel at 10 to 700 mg/gm. A person of ordinary skill in the art would have been motivated to formulate an oral dose of paclitaxel at these concentrations in order to achieve a therapeutically effective to of paclitaxel. A person of ordinary skill in the art would have expected success when using paclitaxel at a dose of 10-700mg as it is known that a

dose of 2-30 mg/kg is required to be effective in treating paclitaxel responsive disease. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (571) 272-0959. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
February 23, 2004
SKS

Christopher S. F. Low
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